Association between Air Pollution and Low Birth Weight: A Community-based Study

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The relationship between maternal exposure to air pollution during periods of pregnancy (entire and specific periods) and birth weight was investigated in a well-defined cohort. Between 1988 and 1991, all pregnant women living in four residential areas of Beijing were registered and followed from early pregnancy until delivery. Information on individual mothers and infants was collected. Daily air pollution data were obtained independently. The sample for analysis included 74,671 first-parity live births with gestational age 37–44 weeks. Multiple linear regression and logistic regression were used to estimate the effects of air pollution on birth weight and low birth weight (<2,500 g), adjusting for gestational age, residence, year of birth, maternal age, and infant gender. There was a significant exposure–response relationship between maternal exposures to sulfur dioxide (SO_2) and total suspended particles (TSP) during the third trimester of pregnancy and infant birth weight. The adjusted odds ratio for low birth weight was 1.11 (95% CI, 1.06-1.16) for each 100 $\mu g/m^3$ increase in SO_2 and 1.10 (95% CI, 1.05-1.14) for each 100 $\mu g/m^3$ increase in TSP. The estimated reduction in birth weight was 7.3 g and 6.9 g for each 100 $\mu g/m^3$ increase in SO_2 and in TSP, respectively. The birth weight distribution of the high-exposure group was more skewed toward the left tail (i.e., with higher proportion of births <2,500 g) than that of the low-exposure group. Although the effects of other unmeasured risk factors cannot be excluded with certainty, our data suggest that TSP and SO_2, or a more complex pollution mixture associated with these pollutants, contribute to an excess risk of low birth weight in the Beijing population. *Key words*: air pollution, birth weight, low birth weight, prospective study, sulfur dioxides, SO_2, total suspended particulates (TSP). *Environ Health Perspect* 105:514–520 (1997)

In both developed and developing countries, low birth weight is the most important predictor for neonatal mortality and is a significant determinant of postneonatal mortality and morbidity (*1,2*). Birth weight represents an endpoint of intrauterine growth, which depends on maternal, placental, and fetal factors, as well as a sequence of constitutional and environmental influences (*3*). An extensive list of risk factors for low birth weight has been reviewed (*4,5*), including maternal age, parity, prepregnancy weight, history of adverse pregnancy outcomes, low social class, and cigarette smoking.

Recent investigations on adverse pregnancy outcomes have paid special attention to occupational risk factors because a growing number of women work outside their homes and there is a concomitant sharp increase in the number of women who work during their pregnancies. Those risk factors examined include employment in certain industries (*6,7*); maternal physical effort and posture (*8*) and prolonged standing (*9*); exposure to polychlorinated biphenyls (PCBs) (*10*), noise (*11*), lead (*12*), and anesthesia gas (*13*); shift work (*14,15*); and job stress (*16*).

A large body of literature has documented both acute and chronic adverse health effects of air pollution. The health end points include mortality (*17–19*), respiratory symptoms (*20,21*), pulmonary function (*22,23*), physician office visits (*24*), and emergency room visits (*25,26*). However, air pollution is not usually considered a possible determinant of pregnancy outcomes. Recently, an ecological study in the Czech Republic (*27*) reported an association between infant mortality and total suspended particulates (TSP), and, to a lesser degree, sulfur dioxide (SO_2). A cross-sectional study in China (*7*) found that the use of coal stoves for heating was significantly associated with low birth weight or preterm birth. Although the data cannot be used to either support or refute a causal inference between air pollution and adverse pregnancy outcomes, it did bring forward some associations that warrant further investigation.

The purpose of this study was to examine the timing and intensity of exposure to TSP and SO_2 during pregnancy and its association with birth weight in a well-characterized cohort, with control for confounding variables. From 1988 to 1991, all pregnant women living in the Dongcheng, Xicheng, Congwen, and Xuanwu areas of Beijing were registered in their local maternal health care center and followed from early pregnancy until delivery. Individual information on both mothers and infants was collected. Daily air pollution data were obtained independently. The analyses borrowed the strength of the time–series approach while offsetting major limitations in many previous time–series studies, i.e., lack of individual information and reliable denominators from which the cases were derived.

Methods

Study area. Dongcheng, Xicheng, Congwen, and Xuanwu are four adjacent residential areas in the center of Beijing (Fig. 1), covering an area of 45 km^2. The total population in 1988 was 2,410,360 (641,853 in Dongcheng, 769,900 in Xicheng, 427,449 in Congwen, and 571,158 in Xuanwu), with 1,223,164 males and 1,187,196 females, constituting approximately 35% of the urban population of Beijing. Sociodemographic characteristics, lifestyle, and housing conditions are compatible among the four areas. There are no major industries, and bicycles are the primary form of transportation. Coal stoves, used for heating or cooking in 97% of households, are the major source of air pollution in the areas (*23*). The residential populations are very stable.

Subjects. The study cohort consisted of all pregnant women who resided in the four areas and delivered live births from 1988 to 1991. In an effort to improve perinatal outcomes, a perinatal health care system was established, under which all resident pregnant women were required to register at their local maternal health care center within 3 months of becoming pregnant. Each

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pregnant woman received a manual with instructions for prenatal and postnatal care and forms for obstetricians to record her age, parity, medical history, first date of last menstrual cycle, prenatal visits, date of delivery, and pregnancy outcomes, including infant sex, birth weight, and gestational age. After delivery, mothers returned to local maternal health care centers where the health care workers arranged a series of postnatal visits based on the information recorded on the returned manual. In China, couples must apply for birth permission from the family planning administration before they may conceive. Because the majority of women are in their first planned pregnancy, a healthy mother and healthy baby are of great concern. More than 95% of pregnant women registered with their health care practitioner within the first trimester of pregnancy. Those women were, in general, able to report an accurate date of last menstrual period. The regionalized prenatal care and delivery service made it possible to have a nearly complete followup of all women from early pregnancy to delivery.

From 1988 to 1991, the maternal health care centers in Dongcheng, Xicheng, Congwen, and Xuanwu received a total of 83,998 manuals. Of 82,750 births with information on parity, the first-parity births accounted for 96.5%. Of 79,828 first-parity births, 235 were missing gestational age, 1,099 missing birth weight, 1,225 missing both gestational age and birth weight, 105 missing infant gender, 40 missing maternal age, and 4 had sex anomalies (ambiguous genitalia and sex could not be determined). Only seven women were under 20 years of age. Of 77,114 first-parity births with complete information on the above variables, the rate of preterm births (gestational age <37 weeks) was 3.2%. Of 74,675 full-term first-parity births, 2 had a gestational age >44 weeks and 2 had birth weight <1000 g.

Air monitoring data. The outdoor TSP and SO_2 concentrations were monitored at the World Health Organization Global Environmental Monitoring System (GEMS) sites in Dongcheng and Xicheng (Fig. 1). Daily air samples were collected and analyzed for 2–3 weeks each month starting in the second week of the month. TSP was measured gravimetrically and SO_2 was measured by colorimetric pararosaniline methods (*28*).

Statistical methods. In this analysis, the means of TSP and SO_2 concentrations measured at the two monitors were used as daily air pollution levels. The daily measurements of the pollutants were highly correlated between the two monitors (Pearson correlation coefficients: 0.93 for TSP and 0.92 for SO_2). To examine the relative importance of timing and magnitude of exposure to air pollution in relation to birth weight, the following exposure variables were constructed for TSP and SO_2: 1) mean level of exposure from last menstrual period to delivery, which allows assessment of exposure level during the entire pregnancy; 2) mean level of exposure during each trimester of pregnancy, which allows assessment of the exposure level during the different gestational stages; and 3) the lagged moving average of exposure, i.e., 1, 2, 3, ... *n* weeks before birth, which allows assessment of exposure level at various proximities from delivery. These exposure variables were evaluated individually and jointly as predictors of birth weight.

In assessing the effects of air pollution on birth weight in a population, two important parameters need to be considered. First, does air pollution universally affect all the births, which can be measured by reduced mean birth weight? Second, does air pollution more likely affect births at the lower end, in which percentage of low birth weight may be a more sensitive indicator than mean birth weight? Thus, in this study, birth weight was modeled both as a binary indicator and as a continuous variable.

Gestational age is the most important determinant of birth weight (*29*). Smoothing plots using generalized additive modeling techniques (*30,31*) were first produced to determine the functional relation between birth weight and gestational age. Consistent with a previous study (*29*), our analysis (limited to 37–44 weeks of gestation) found the relationship between birth weight and gestational age to be nonlinear. Within this age range, a linear and a quadratic term of gestational age appear to fit the data well and thus are included in all the regression models.

Multiple logistic regression was performed to assess the effects of TSP and SO_2 on the risk of low birth weight (<2,500 g), with adjustment for gestational age and indicators of season, residential area, maternal age (20–24, 25–29, 30+ years), and infant gender. Stratified analyses by residence, maternal age, season, year of birth, and infant sex were also performed to evaluate the consistency of the associations across strata.

Finally, multiple linear regression was used to estimate the effects of TSP and SO_2 on birth weight. Because gestational age is the most important determinant of birth weight, it was controlled in the model to evaluate if the effects of air pollution on birth weight are through shorter gestation or slower intrauterine growth in addition to all other covariates.

Results

In this report, the sample for analysis included 74,671 first-parity single live births with gestational age between 37 and 44 weeks and with birth weight >1,000 g, who had complete records, and whose mothers were 20 years of age or older at the start of pregnancy. The characteristics of these births are summarized in Table 1. The overall mean birth weight was 3,318 g [standard deviation (SD) = 428] and the rate of low birth weight (<2,500 g) was 2.9%. However, the mean birth weight and the rate of low birth weight varied by residence, season, maternal age, infant sex, and year of birth. It is noted that there is a trend of decreasing number of annual births. The possible reasons include a

Figure 1. Geographic locations of the four study areas: Xicheng, Dongcheng, Xuanwu, and Chongwen. The circled numbers mark the sites of World Health Organization air monitoring stations in Beijing.

Table 1. Mean birth weight and rate of low birth weight (<2,500 g) in first-parity live births with gestational age 37–44 weeks in four residential areas of Beijing

Characteristic	No. of live births	Birth weight (g) Mean	SD	<2,500 g (%)
Total	74,671	3,318	428	2.94
Residential area				
Dongcheng	21,450	3,314	427	3.02
Xicheng	23,720	3,332	425	2.58
Congwen	15,612	3,319	430	3.11
Xuanwu	13,889	3,298	432	3.23
Season				
Spring	19,566	3,319	431	3.09
Summer	19,664	3,327	422	2.59
Autumn	16,470	3,332	425	2.57
Winter	18,971	3,294	432	3.46
Maternal age (years)				
20–24	14,600	3,316	423	2.87
25–29	49,804	3,321	426	2.78
30+	10,267	3,305	443	3.82
Sex of infant				
Male	39,056	3,367	430	2.45
Female	35,615	3,264	419	3.48
Year of birth				
1988	24,050	3,300	425	3.14
1989	20,683	3,310	425	3.11
1990	19,541	3,342	429	2.54
1991	10,397	3,328	435	2.89

SD, standard deviation.

decreasing number of women aged 20–35 years as baby boomers age; more and more couples postponing childbearing; and women who were pregnant in 1991 but delivered in 1992 were not included.

Figure 2 plots mean TSP and SO_2 levels and mean birth weight by month from 1987 to 1991. The air pollution levels were the mean of daily air pollution levels for the month. Superimposed on the air pollution levels is the mean birth weight of all live births occuring in each corresponding month. There were clear seasonal patterns for both air pollution level and mean birth weight. The TSP and SO_2 levels were highest around January and lowest around July. There was a crude inverse relationship between air pollution level and mean birth weight, i.e., high air pollution levels corresponded to reduced birth weight, and vice versa. A similar relationship was found between air pollution level and rate of low birth weight (data not shown).

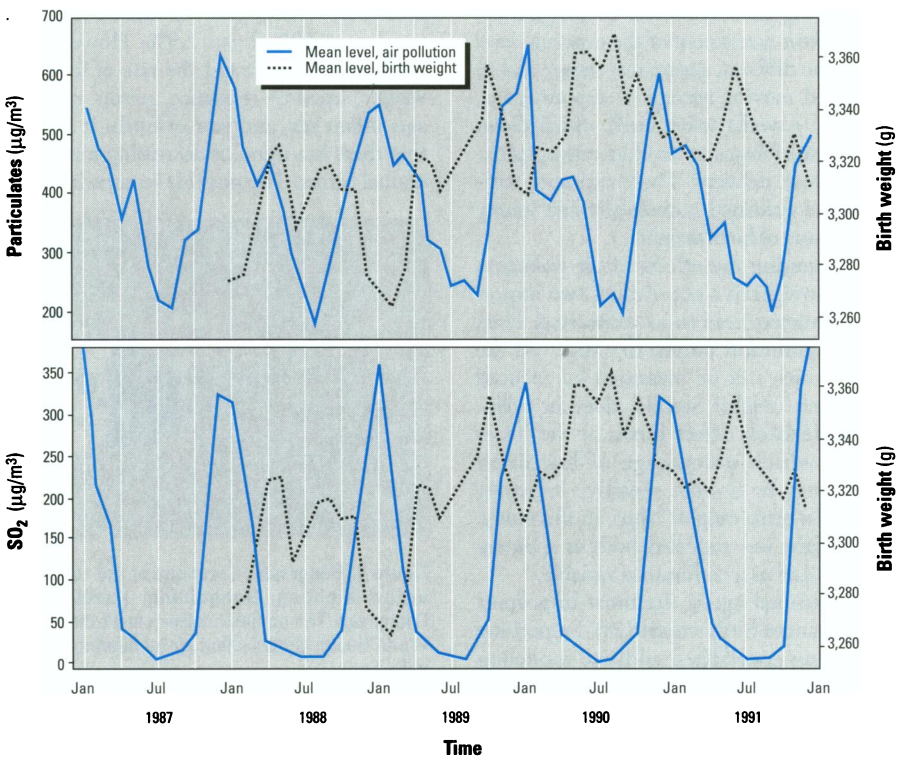

Figure 2. Plot of mean birth weight and total suspended particles (TSP) and SO_2 concentrations, by month from 1987 to 1991.

Table 2. Estimated ORs and 95% CIs of low birth weight (<2,500 g) by quintiles of maternal exposure to TSP and SO_2 during the third trimester of pregnancy in first parity live births with gestational age 37–44 weeks

	SO_2			TSP	
Exposure	OR	95% CI	Exposure	OR	95% CI
Crude quintile indicators[a]					
9–18 μg/m³ (Ref)			211–280 μg/m³ (Ref)		
18–55	1.13	0.98–1.31	280–361	0.92	0.79–1.06
55–146	1.15	1.00–1.33	361–437	1.09	0.95–1.25
146–239	1.20	1.04–1.38	437–498	1.19	1.04–1.37
239–308	1.40	1.23–1.61	498–618	1.23	1.07–1.40
Continuous variables[b]	1.10	1.06–1.15		1.10	1.05–1.14
Adjusted quintile indicators[c]					
9–18 μg/m³ (Ref)			211–280 μg/m³ (Ref)		
18–55	1.09	0.94–1.26	280–361	0.91	0.78–1.05
55–146	1.12	0.97–1.29	361–437	1.08	0.94–1.25
146–239	1.16	1.01–1.34	437–498	1.15	1.00–1.32
239–308	1.39	1.22–1.60	498–618	1.24	1.08–1.42
Continuous variables[b]	1.11	1.06–1.16		1.10	1.05–1.14

Abbreviations: OR, odds ratio; CI, confidence interval; TSP, total suspended particles; Ref, reference value.
[a]Logistic regression models adjusted for gestational age.
[b]Linear trend test, $p<0.01$, for each 100 μg/m³ increase in TSP or SO_2.
[c]Logistic regression models adjusted for gestational age, residential area, maternal age, year of birth, and infant gender.

The associations between air pollution and the risk of low birth weight were further evaluated by logistic regression models. To examine the relative importance of timing and magnitude of exposure to air pollution in relation to birth weight, the following exposure variables were considered for TSP and SO_2: 1) mean level of exposure from last menstrual period to delivery, 2) mean level of exposure during each trimester of pregnancy, and 3) the lagged moving average of exposure, i.e., 1, 2, 3, ... *n* weeks before birth. These exposure variables were evaluated individually and jointly as predictors of low birth weight. The best-fitting models for low birth weight included the mean level of exposure to TSP and SO_2 during the third trimester of pregnancy. After adjustment for the third trimester exposure, other exposure variables (exposure during the entire pregnancy and the lagged moving average) had little predictive value. There was a small negative association between exposures in the first and second trimester of pregnancy and risk of low birth weight, which was independent of the effect of the third trimester exposure. This finding will be elaborated in the discussion section.

The following analyses focused on the third trimester exposures. Two types of exposure variables in the third trimester of pregnancy were considered: the mean exposure from 25 to 36 weeks of gestation and the mean exposure from 25 weeks of gestation to delivery. The two variables were found to be equally good predictors of birth weight. The subsequent analysis used the mean exposure from 25 weeks of gestation to delivery.

As shown in Table 2, the crude odds ratios of low birth weight increase with each quintile of SO_2 and TSP exposure during the third trimester of pregnancy. The risk of low birth weight was significantly increased for those infants whose mothers had high levels of exposure (4th and 5th quintiles of TSP or SO_2). The above estimates were not altered by control for residence, maternal age, year of birth, and infant sex (Table 2). The data suggest an exposure–response relationship between air pollution and low birth weight (Fig. 3): the higher the TSP or SO_2 levels, the higher the risk of low birth weight. A linear trend test of the association on the logistic scale was highly significant: odds ratios increased by a factor of 1.11 for each 100 µg/m^3 increase in SO_2 and 1.10 for TSP. The risk predicted by this model for an exposure of 300 µg/m^3 in SO_2 is $1.11^3 = 1.37$ and for an exposure of 600 µg/m^3 in TSP is $1.10^6 = 1.77$. With further adjustment for season, the point estimates remain almost unchanged, but the CIs of the estimates become wider. For example, for each 100 µg/m^3 increase in exposure, the odds ratio is 1.12 (CI, 1.03–1.22) for SO_2 and 1.10 (CI, 1.01–1.20) for TSP, due to the colinearity between season and air pollution level. There is also a high degree of correlation between TSP and SO_2 as shown in Figure 2. Thus, it is difficult to determine whether one is a more important factor than the other.

Stratified logistic regression analyses by residence, season, maternal age, infant sex, and year of birth were performed (Table 3). The overall trends of the associations of TSP and SO_2 on birth weight were consistent across the strata; however, the magnitude of the effects varied. The effects of TSP and SO_2 on birth weight were statistically significant in both summer and winter. Although the air pollution level was much higher in winter than in summer (Fig. 2), the odds ratios for SO_2 were greater in summer than in winter. The effects of SO_2 and TSP on birth weight were smaller among younger (<25 years) and older mothers (>29 years), which may be attributable to sparse data at the two extreme ages. Some gender difference in the effects of TSP and SO_2 was noticed, with the effects greater in males than in females.

The associations of air pollution with birth weight were evaluated by multiple linear regression. Again, the crude and the adjusted estimates were similar (Table 4). Higher exposures to TSP and SO_2 were associated with reduced birth weight. A linear trend test of the association was statistically significant. After adjustment for gestational age and other covariates, the estimated reduction in birth weight was 7.3 and 6.9 g for each 100 µg/m^3 increase in SO_2 and TSP, respectively.

Finally, birth weight distributions were compared by tertiles of TSP and SO_2 levels (Fig. 4,5). The difference in birth weight distributions between low and high exposed groups was clear in the left tail; i.e., the higher the level of exposures, the higher the proportion of babies with birth weight <2,500 g.

Discussion

Literature on the association of air pollution with pregnancy outcomes has been very limited. The ecological study in the Czech Republic (*27*) reported a weak association of air pollution on neonatal mortality and postneonatal nonrespiratory mortality. However, much more substantial associations were observed for postneonatal respiratory mortality, and the highest to lowest quintile risk ratios were 2.41 (95% CI, 1.10–5.28) for TSP and 3.91 (95% CI, 0.90–16.9) for SO_2. The cross-sectional

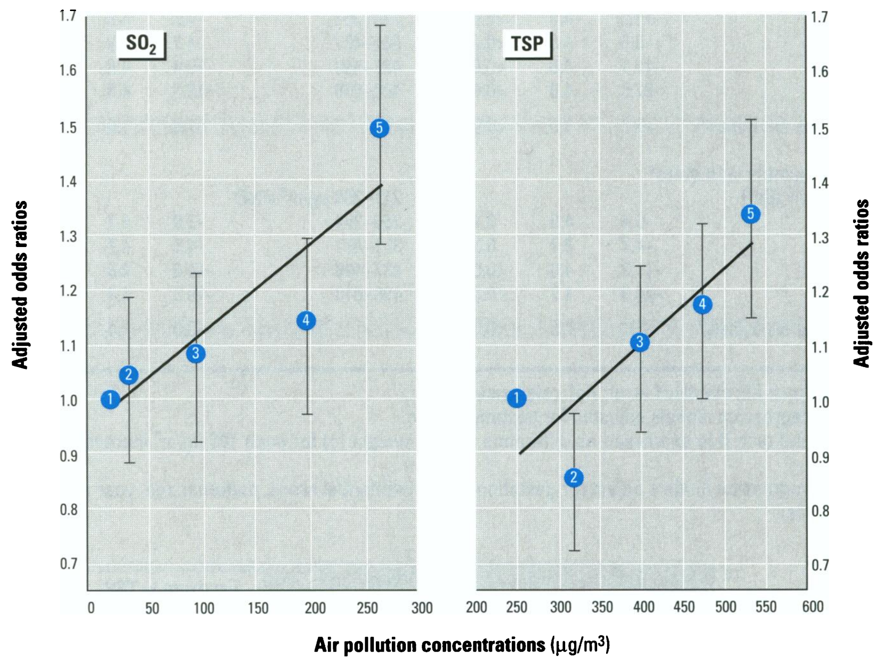

Figure 3. Adjusted odds ratios and their 95% confidence intervals by quintiles of SO_2 and total suspended particles (TSP) concentrations in the third trimester of pregnancy. The plots were derived from logistic regressions, with adjustment for gestational age, residence, year of birth, maternal age, and infant sex.

Table 3. Effects[a] of maternal exposures to SO_2 and total suspended particles (TSP) during pregnancy on low birth weight (<2,500 g) in first-parity live births with gestational age 37–44 weeks, stratified by residential area, seasons, and maternal age

	SO_2		TSP	
Stratified factors	OR	95% CI	OR	95% CI
Residential area				
Dongcheng	1.21	1.03–1.42	1.26	1.07–1.48
Xicheng	1.08	0.92–1.26	0.98	0.83–1.15
Congwen	1.13	0.94–1.36	1.07	0.88–1.29
Xuanwu	1.04	0.86–1.26	1.10	0.91–1.34
Season				
Summer (May–October)	1.28	1.11–1.49	1.16	1.06–1.27
Winter (November–April)	1.14	1.06–1.23	1.10	1.02–1.18
Maternal age (years)				
20–24	1.04	0.86–1.26	1.06	0.87–1.29
25–29	1.18	1.06–1.31	1.15	1.03–1.29
30+	1.03	0.84–1.27	1.00	0.81–1.23
Sex				
Male	1.16	1.02–1.32	1.15	1.01–1.32
Female	1.09	0.97–1.22	1.07	0.95–1.20
Year of birth				
1988	1.14	0.99–1.31	1.15	1.00–1.33
1989	1.37	1.15–1.64	1.38	1.11–1.71
1990	1.01	0.85–1.19	1.00	0.85–1.18
1991	0.99	0.76–1.28	1.01	0.78–1.31

Abbreviations: OR, odds ratio; CI, confidence interval. ORs are expressed per 100 µg/m^3 increase in SO_2 or TSP.

[a]Logistic regression models adjusted for gestational age, season, residential area, maternal age, year of birth, and infant gender (except for the stratified variable).

Table 4. Effects of maternal exposure to total suspended particles (TSP) and SO_2 during the third trimester of pregnancy on birth weight (g) in first-parity live births with gestational age 37–44 weeks

	SO_2				TSP		
Exposure	β	SE	*p*-value	Exposure	β	SE	*p*-value
Crude quintile indicators[a]							
9–18 μg/m³ (Ref)				211–280 μg/m³ (Ref)			
18–55	-12.9	4.8	<0.01	280–361	-4.5	4.8	0.34
55–146	-9.6	4.8	<0.05	361–437	-4.7	4.8	0.33
146–239	-15.1	4.8	<0.01	437–498	-19.4	4.8	<0.01
239–308	-27.0	4.8	<0.01	498–618	-19.3	4.8	<0.01
Continuous variables[b]	-7.3	1.5	<0.01		-7.6	1.5	<0.01
Adjusted quintile indicators[c]							
9–18 μg/m³ (Ref)				211–280 μg/m³ (Ref)			
18–55	-6.4	4.8	0.18	280–361	-3.0	4.7	0.52
55–146	-4.7	4.7	0.32	361–437	-4.5	4.7	0.35
146–239	-11.2	4.8	<0.05	437–498	-14.5	4.8	<0.01
239–308	-24.3	4.7	<0.01	498–618	-19.3	4.8	<0.01
Continuous variables[b]	-7.3	1.5	<0.01		-6.9	1.4	<0.01

Abbreviations: SE, standard error; Ref, reference value.
[a]Multiple regression models adjusted for gestational age.
[b]Linear trend test; β is expressed as difference in birth weight (g) for each 100 μg/m³ increase in TSP or SO_2.
[c]Multiple regression models adjust for gestational age, residential areas, maternal age, year of birth, and infant gender.

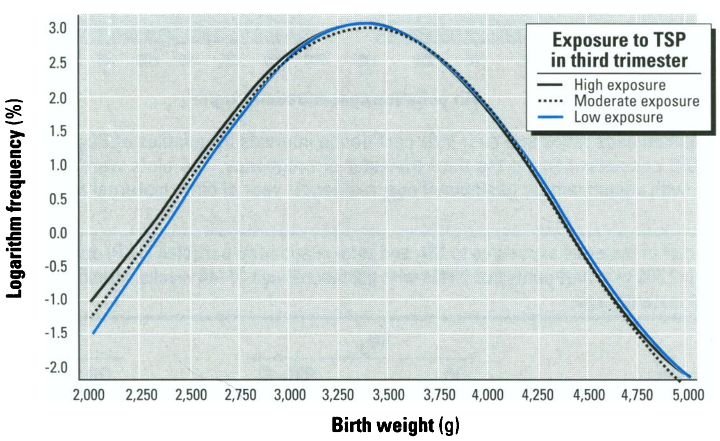

Figure 4. Birth weight distributions by tertiles of mean total suspended particles (TSP) concentrations in the third trimester of pregnancy. Logarithm scale was used to emphasize the tail of the curve.

study in China (*7*) found an association between use of indoor coal stoves for heating and low birth weight or preterm birth, with an odds ratio of 1.40 (95% CI, 1.03–1.91). Our recent report (*32*) showed that TSP and SO_2 are associated with excessive risk of preterm births in this population. The adjusted odds ratio for preterm births was 1.21 (95% CI, 1.01–1.46) for each ln 100 μg/m³ increase in SO_2 and 1.10 (95% CI, 1.01–1.20) for each 100 μg/m³ increase in TSP. To our knowledge, the present study is the first to employ a time–series approach to assess maternal exposures to TSP and SO_2 during pregnancy in relation to birth weight. This study has several strengths. First, it is community based; thus, it is less likely to suffer selection bias, healthy worker effects, or attrition than an occupationally based study. Second, the data on gestational age and birth weight are reliable and accurate because they are collected prospectively from the beginning of pregnancy and verified by obstetricians. Third, daily TSP and SO_2 measurements were obtained independently from air monitoring stations. Finally, this is a well-defined cohort with information on individual characteristics and reliable denominators.

In this study, we found a significant exposure–response relationship between maternal exposures to SO_2 and TSP during the third trimester of pregnancy and infant birth weight, after adjustment for gestational age, residence, year of birth, maternal age, and infant sex. The adjusted odds ratio for low birth weight (<2,500 g) was 1.11 (95% CI, 1.06–1.16) for each 100 μg/m³ increase in SO_2 and 1.10 (95% CI, 1.05–1.14) for each 100 μg/m³ increase in TSP. The estimated reduction in birth weight was 7.3 g and 6.9 g for each 100 μg/m³ increase in SO_2 and TSP, respectively. The associations were statistically significant in both winter and summer, although greater in summer. In addition, the birth weight distribution of the high-exposure group was skewed more toward the left tail (i.e., with higher proportion of births <2,500 g) than that of the low-exposure group. The data suggest that those pregnancies at high risk for low birth weight may be particularly susceptible to the adverse effects of air pollution. In studying the association of air pollution with birth weight, investigators should pay special attention to the left tail of the birth weight distribution. All these analyses provide coherent evidence that air pollution may contribute to reduced birth weight and an excess risk of low birth weight in this population.

Several important points are worth mentioning. If we simply examine mean birth weight, the effects of air pollution were statistically significant but small in magnitude. In comparison, there have been numerous reports of the effects of maternal smoking on birth outcomes. Infants born to smoking mothers weigh on average 200 g less than infants of nonsmokers (*33*). The magnitude of effects of maternal passive smoking is much smaller, and studies so far have yielded mixed results (*33*). However, if we evaluate air pollution in relation to rates of low birth weight, its effects cannot be ignored. For example, with the lowest quintile of SO_2 as the reference, the adjusted weighted relative risk of low birth weight from the logistic regression model (*34*) was 1.19 among women exposed to higher quintiles of SO_2. The attributable risk (the proportion of low birth weight in this sample that was attributable to air pollution) was 13%. This is among the largest attributable risks ever reported for the known risk factors of low birth weight. From the public health point of view, the impact of air pollution on birth weight is profound.

Fetal growth does not follow a uniform pattern. Rather, it represents different periods of growth spurts for different organs and anthropometric measurements (*35*). Thus, the time, intensity, and duration of the negative factors affecting fetal growth will manifest themselves in differing patterns. Previous studies (*35*) indicate that the peak fetal length growth occurs first, around the 20th week of gestation, while peak weight growth occurs around 33 weeks of gestation. It is estimated that by the 28th week, length has reached 71% of the mean length at term (41 weeks), while weight is only 32% of the full-term infant weight (*36*). In other words, weight growth is predominantly a phenomenon of the third trimester. The present study found consistently that the mean level of maternal exposures to TSP and SO_2 during the third trimester of pregnancy is the best predictor of reduced birth weight. Our findings also imply that the effects of air pollution on birth weight appear to be cumulative. We noticed a small negative association between exposures in the first and second trimesters of pregnancy and low birth weight. This negative relationship does not imply a protective effect of air pollution during early pregnancy; rather, it may be attributed to several possibilities. First, because of the distinct seasonal pattern of air pollution, the level of exposure in the first and second trimesters is almost always inversely associated with that of the third trimester. Second, the effects of air pollution on pregnancy outcomes may differ by the timing of exposure, i.e., early exposure may be more important for pregnancy end points such as spontaneous abortion and birth defects, which are not considered in this analysis. Third, this study is limited to full-term live births; thus, the birth weights of those fetuses who did not survive to term or were born prematurely are excluded from the analysis. However, those compromised fetuses may be disproportionately affected by air pollution during the first or second trimester of pregnancy.

Low birth weight may be attributed to preterm delivery or intrauterine growth retardation or a combination of both. Although preterm and intrauterine growth-retarded infants can have similar birth weights, they are known to show differential neonatal and postneonatal features (*37*), thereby suggesting differential etiology involved in the two conditions. This present analysis is limited to full-term live births for two reasons: first, to obtain complete exposure assessment for each trimester of pregnancy, and second, to assess the effect of air pollution in a more homogeneous sample. Because gestational age was included in all the models, the regression coefficients should be interpreted as the effects of air pollution on gestational age-specific birth weight. The data from our previous report (*32*) and present analyses appear to indicate that exposure to high levels of TSP and SO_2 is associated with both reduced gestational age and gestational age-specific birth weight. It is possible that maternal exposure to air pollution during pregnancy may also affect other pregnancy endpoints, including spontaneous abortion, fetal death, and preterm delivery. These endpoints may be more sensitive to exposure in early pregnancy and warrant consideration in future studies.

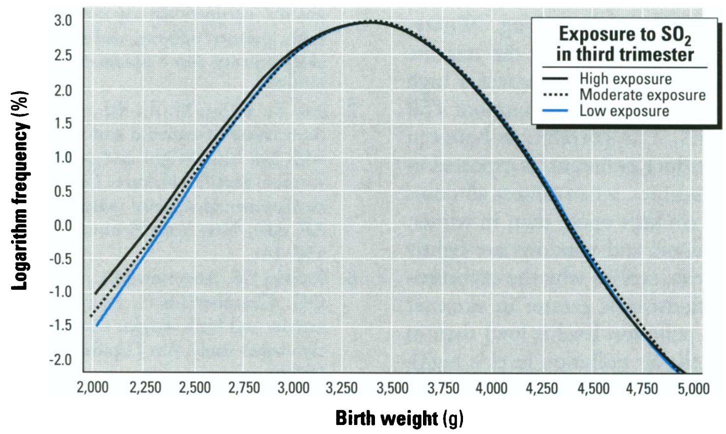

Figure 5. Birth weight distributions by tertiles of mean SO_2 concentrations in the third trimester of pregnancy. Logarithm scale was used to emphasize the tail of the curve.

The biological mechanisms whereby air pollution is associated with low birth weight remain to be determined. Respiratory health effects of inhaled pollutants depend on their depth of penetration, deposition, and retention in the lung, as well as on the subsequent biological responses induced by the deposited material (*38*). In comparison, a mechanism for air pollution to affect birth weight is less straightforward. Fetal growth is influenced by maternal, placental, and fetal factors. Air pollution may affect maternal respiratory or general health, which may in turn impair uteroplacental and umbilical blood flow, transplacental glucose, and total insulin, the major determinants of fetal growth (*39*). Besides SO_2 and TSP, the major pollutants from coal combustion include carbon monoxide, carbon dioxide, and volatile organic compounds. These pollutants may be absorbed into the maternal bloodstream, cross the placental barrier, and have direct toxic effects on the fetus.

This study is limited in several respects. A number of factors that are known or suspected to affect birth weight, such as maternal nutrition and prepregnancy weight and weight gain (*40*), cigarette smoking (*41*), history of adverse pregnancy outcomes (*29*), and occupational exposures (*6–16*), could not be examined. However, because these factors are expected to be independent of daily air pollution levels, the estimated effects of air pollution are likely to be free of confounding by these factors. This is supported by our data in which the estimated effects of air pollution on birth weight were not significantly altered by the inclusion or exclusion of indicator variables for other risk factors in our model, including residence, season, year of birth, maternal age, and infant gender. Although maternal smoking is an important risk factor of low birth weight, the smoking prevalence in Chinese women is extremely low, especially in large cities. According to the 1984 national smoking survey, 93.6% of women aged 20–60 years were nonsmokers (*42*). Thus, maternal smoking status should not be a significant confounder in this cohort.

Most studies on acute health effects of air pollution control for meteorological factors, including daily temperature and humidity. In this study, analyses were performed with and without adjustment for season for several reasons: 1) in this cohort birth weight represents an endpoint of 37–44 weeks of gestation, not an acute event; 2) there is well-documented seasonality of birth outcomes with unknown etiology; 3) Beijing has distinct winter and summer seasons in terms of temperature, humidity, and wind; and 4) season is also correlated with outdoor activities, household ventilation, types of foods available, etc. Adjustment for season, therefore, may also help to control for potential confounders that covary with season. Further adjustment for season did not significantly alter the results.

In this study, only outdoor TSP and SO_2 levels were available; there was no simultaneous measurement of indoor air pollution. If indoor air pollution levels differed substantially from outdoor levels, lack of indoor air pollution control in the analysis of outdoor air pollution could diminish the power to detect the significance in effects because of potential measurement errors in individual exposures. However, according to our previous study (*21*), the principal source of ambient pollution in this area is coal combustion for heating and cooking. Ninety-seven percent of households in the area use this fuel; therefore, one can expect a high correlation between indoor and outdoor TSP and SO_2 levels. The correlation between indoor and outdoor pollutants is expected to be higher in summer, when almost all doors and windows are kept open, than in winter, when all the doors and windows are tightly sealed. This helps explain why the exposure–response relationship is greater in summer (when the air pollution level is low) than in winter (when the air pollution level is high). This is why there is a lesser degree of exposure misclassification in summer than in winter.

Finally, in this study we examined only TSP and SO_2, as they are the only two pollutants monitored under GEMS. Because TSP and SO_2 may be highly correlated with other pollutants emitted from the same source, we cannot rule out the possibility that TSP and SO_2 are simply surrogates for a complex mixture of air pollutants. A more accurate method of assessing the effects of individual pollutants would be human chamber studies, which have been used to assess the acute effects of short-term exposure (*38*). However, the methods are not feasible for pregnant women. In addition, it has been recognized that the actual composition, physical state, and size distribution of particulates may profoundly affect their toxic action (*43*). A TSP level itself does not reveal any distinction in terms of particulate size and composition. The proportion and components of respirable particles could vary greatly in different seasons and areas. Better exposure assessment is needed in future studies.

In summary, although the effects of other unmeasured risk factors cannot be excluded with certainty, our data suggest that intrauterine exposure to TSP and SO_2, or a more complex pollution mixture associated with these pollutants, contributes to excess risk of low birth weight in this population.

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